"consisting of" thereby excluding all other active pharmaceutical agents, yet. Applicant respectfully traverses the objection. Applicant respectfully submits that the Examiner has failed to consider the full scope of claim 1.

Claim 1 is directed to a method of treating an autoimmune disease of the mouth comprising topically contacting the mouth of a patient in need of such treatment with a formulation consisting of the following components: (i) a pharmaceutically acceptable carrier, (ii) a member selected from the group consisting of azathioprine, 6-mercaptopurine, 6-thioguanine nucleotide, and pharmaceutically acceptable salts thereof, and optionally (iii) a non-steroidal anti-inflammatory agent. The term "optionally" is used to define alternative members of the formulation employed in claim 1. The formulation employed in the method of claim 1 may consist of, therefore, components (i) and (ii) or components (i), (ii) and (iii).

Applicant respectfully submits that the use of "optionally" is acceptable under 35 U.S.C. § 112, second paragraph because there is no ambiguity as to which alternatives are covered by the claim. *See* MPEP § 2173.05(h). In accordance with 37 C.F.R. § 1.75(c), claims 37-39 limit the scope of claim 1 by reciting specific non-steroidal anti-inflammatory agents. In view of claims 37-39 further limiting the optional anti-inflammatory agent of claim 1, Applicant respectfully submits that the objection to claims 37-39 under 37 C.F.R. § 1.75(c) as being of improper form for failing to further limit the subject matter of claim 1 is improper and should be withdrawn.

than 37-39 should not say further comprising

B. Patentability Arguments

1. 35 U.S.C. § 112, Second Paragraph

a. The rejection of claims 19, 21-28 and 30-36 under 35 U.S.C. § 112, second paragraph

At page 2 of Paper 13, claims 19, 21-28 and 30-36 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant respectfully traverses the rejection.

At page 3 of Paper 13, the Examiner alleges that the expression, "a method of preventing an autoimmune disease of the mouth" in claim 19, line 1 renders the claim indefinite as failing to clearly set forth the metes and bounds of the patent protection desired. The Examiner alleges

that the specification does not set forth how and when to prevent autoimmune disease of the mouth. Applicant respectfully points out that the application discloses that azathioprine may be administered prior to the onset of an autoimmune disease to inhibit development of the symptoms associated with an autoimmune disease. *See* page 8, lines 21-23. For example, the application discloses that azathioprine may be administered prior to or after a bone marrow transplant before symptoms of aGVHD or cGVHD develop. *See* page 9, lines 1-2. In view of the application identifying situations that an autoimmune disease of the mouth may be prevented, Applicant respectfully submits that the rejection of claims 19, 21-28 and 30-36 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention is improper and should be withdrawn.

2. 35 U.S.C. § 102(b)

a. The rejection of claims 1, 3-4, 8 and 17 for lack of novelty over Eggleston *et al.*

At page 3 of Paper No. 13, claims 1, 3-4, 8 and 17 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Eggleston. The Examiner characterizes Eggleston as disclosing a method of treating aphthous ulceration employing topical azathioprine pellets. Applicant respectfully traverses the rejection. Applicant respectfully submits that Eggleston does not disclose each and every element of claims 1, 3-4, 8 and 17, as amended.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *See* § MPEP 2131. Claims 1, 3-4, 8 and 17, as amended, are directed to a method of preventing an autoimmune disease of the mouth comprising topically contacting the mouth of a patient in need of such treatment with a formulation consisting of a pharmaceutically acceptable carrier, an effective amount of a member selected from the group consisting of azathioprine, 6-mercaptopurine, 6-thioguanine nucleotide, and pharmaceutically acceptable salts thereof, and optionally a non-steroidal anti-inflammatory agent. In support of claims 1, 3-4, 8 and 17, the application discloses that patients suffering from GVHD demonstrate significant improvement in pain and ulceration upon treatment with an effective amount of azathioprine. *See* page 20, lines 18-21. By contrast, the cited reference does not disclose a method of treating aphthous ulceration employing an effective amount of topical azathioprine pellets because Eggleston discloses that there were "no

significant differences between the drug and the placebo" in the double blind cross-over clinical trial of 26 patients with aphthous ulceration. *See* page 235, ¶¶1-2. In view of Eggleston not disclosing each and every element of claims 1, 3-4, 8 and 17, as amended, Applicant respectfully submits that the rejection of claims 1, 3-4, 8 and 17 under 35 U.S.C. § 102(b) has been overcome and withdrawal thereof is respectfully requested.

3. 35 U.S.C. § 103(a)

a. The rejection of claims 1, 3-10, 12-19, 21-28 and 30-39 under 35 U.S.C. § 103(a) as being obvious over Eggleston in view of Lozada and Sharpe

At page 4 of Paper No. 13, claims 1, 3-10, 12-19, 21-28 and 30-39 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Eggleston in view of Lozada and Sharpe. Applicant respectfully traverses the rejection. At page 5 of Paper No. 13, the Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ azathioprine (an immunosuppressive agent), and corticosteroids in a topical formulation employed in a method of treating autoimmune diseases of the mouth. At page 5 of Paper No. 13, the Examiner also alleges that it would have been obvious to employ NSAIDs in the methods. Applicant respectfully submits that the Examiner has not established a prima facie case of obviousness.

To establish a prima facie case of obviousness under 35 U.S.C. § 103, the following three criteria must be met: (i) the cited prior art references when combined must teach or suggest all the claim limitations; (ii) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings; and (iii) there must be a reasonable expectation of success. *See* MPEP 2142.

Applicant respectfully submits that the Examiner has not established a prima facie case of obviousness, because the combination of cited prior art references do not teach or suggest all the claim limitations. As discussed above, claim 1 is directed to a method of treating an autoimmune disease of the mouth comprising topically contacting the mouth of a patient in need of such treatment with a formulation consisting of a pharmaceutically acceptable carrier, an immunosuppressive agent such as azathioprine, and optionally an NSAID. The use of the close transitional phrase "consisting of" in claim 1 excludes all other active pharmaceutical agents in the formulation, such as corticosteroids. In view of the combination of cited references

disclosing a formulation containing corticosteroids and the formulation of the claimed invention not consisting of corticosteroids, Applicant respectfully submit that the cited references fail to teach or suggest all the claim limitations.

Applicant respectfully submits that the Examiner has also not established a prima facie case of obviousness, because there is no reasonable expectation of success. In order to arrive at the invention of claim 1 based on the teachings of the cited references, one would have been required to be motivated to remove the corticosteroid component from the formulation. At page 4 of Paper No. 13, the Examiner characterizes Eggleston as teaching a method of treating aphthous ulceration employing topical azathioprine. Applicant respectfully note that the prior art must be considered in its entirety, including disclosures that teach away from the claimed invention. *See* MPEP 2141.02. As discussed above, Eggleston discloses that a non-effective amount of topically administered azathioprine "is of no value in treatment of aphthous ulceration." *See* page 236, ¶ 1. Eggleston also discloses that more than 10% of the test subjects (3/26) had to be removed from the trial because of a sudden increase in the number of ulcers. *See* page 234, ¶ 3. In contemplating the use of higher doses of azathioprine for treating aphthous ulceration, Eggleston discloses that "our experience of three patients whose ulceration rapidly increased while on the active preparation should be borne in mind if larger topical doses are contemplated." *See* page 236, ¶ 1. Eggelston further discloses that "[i]f the disorder has an *autoimmune basis*, patients with severe ulceration may benefit from low-dose *systemic* azathioprine." *See* page 236, ¶ 2 (emphasis added). The disclosure in Eggleston of significant side effects using low doses of azathioprine and the recommendation for using systemic azathioprine to treat autoimmune forms of aphthous ulceration does not lead to a reasonable expectation of success and, in fact, teaches away from the method of claim 1, wherein a formulation consisting of a pharmaceutically acceptable carrier, an immunosuppressive agent such as azathioprine and optionally an NSAID are topically administered to treat an autoimmune disease of the mouth. In view of the cited references not suggesting or teaching all the limitations of claims and in view of the cited references not providing a reasonable expectation of success, Applicant respectfully submits that the rejection of claims 1, 3-10, 12-19, 21-28 and 30-39 under 35 U.S.C. § 103(a) is improper and should be withdrawn.

As the current attorney of record, Lyon & Lyon, is no longer in existence, please direct all further correspondence regarding the above patent application to:

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A Revocation and Appointment of Power of Attorney will be forthcoming.

CONCLUSION

In view of the above remarks, Applicant respectfully submit that the present application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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EXHIBIT A

Pursuant to 37 C.F.R. §1.121(c)(1)(ii), Applicant presents herewith marked-up text of the claims of this application as amended by the foregoing amendment.

1. (Three Times Amended) A method for treating an autoimmune disease of the mouth comprising topically contacting the mouth of a patient in need of such treatment with a formulation consisting of a pharmaceutically acceptable carrier, **an effective amount of** a member selected from the group consisting of azathioprine, 6-mercaptopurine, 6-thioguanine nucleotide, a pharmaceutically acceptable salt of azathioprine, a pharmaceutically acceptable salt of 6-mercaptopurine, and a pharmaceutically acceptable salt of 6-thioguanine nucleotide. and optionally a non-steroidal anti-inflammatory agent.